

Table 2 Continued.

Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<b>Africa</b>			
Institut Pasteur Place Charles-Nicolle Casablanca, Morocco	<u>Cerastes cerastes</u> <u>Vipera lebetina</u>	Antivipérin	
Institut Pasteur 43 Place Pasteur Tunis, Tunisia	<u>Cerastes cerastes</u> <u>Vipera lebetina</u>	Antivipérin	
Al Aigousa Sharra Alvezra Cairo, Egypt	<u>Cerastes cerastes</u> <u>Cerastes vipera</u>	Anti-Vipera	
Naja haje	<u>Cerastes cerastes</u> <u>Cerastes vipera</u>	Polyvalent	
The South African Institute for Medical Research P.O. Box 1038 Johannesburg 2000 Republic of South Africa	<u>Hemachatus haemachatus</u> <u>Naja nivea</u> <u>Naja haje</u> <u>Naja melanoleuca</u> <u>Naja nigriceps</u> <u>Dendroaspis angusticeps</u> <u>Dendroaspis jamesoni</u> <u>Dendroaspis polylepis</u> <u>Bitis arietans</u> <u>Bitis gabonica</u> <u>Echis carinatus</u>	Digested with pepsin and pre- cipitated with ammonium sulphate. Polyvalent	RUSSELL

SNAKE VENOM IMMUNOLOGY

Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<b>Africa</b>			
FitzSimmon's Snake Park P.O. Box 1 Sneil Parade Durban, South Africa	Dendroaspis angusticeps Dendroaspis jamesoni Dendroaspis polylepis  Hemachatus haemachatus Naja nivea Bitis arietans Bitis gabonica	Dendroaspis  polyvalent	Digested with pepsin, precipitated with ammonium sulphate, and dialyzed.
<b>Middle East</b>			
Ministry of Health Dept. of Laboratories P.O. Box 6115 Jerusalem 91060, Israel	Echis coloratus  Vipera balaestinae	Anti-Echis  Anti-Vipera	Whole venom plus resin-bound "neurotoxin" used as antigen. Supplied as globulin fraction of horse serum in liquid form.
Institut d'Etat des Séums et Vaccins Razi P.O. Box 656 Teheran, Iran	Naja naja oxiana  Vipera lebetina	Anti-Cobra  Anti-Lebetina	prepared by pepsin digestion, and ammonium sulphate precipitation.

(Continued)

Table 2 Continued.

Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<b>Middle East</b>			
	<u>Echis carinatus</u>	Anti-Echis	
	<u>Pseudocerastes persicus</u>	Anti-Persica	
	<u>Vipera xanthina</u>	Anti-Latifi	
	<u>Aqkistrodon halys</u>	Anti-Aqkistrodon	
	<u>Naja naja oxiana</u>		
	<u>Vipera lebetina</u>		
	<u>Echis carinatus</u>		
	<u>Pseudocerastes persicus</u>	Polyvalent	
	<u>Vipera xanthina</u>		
	<u>Aqkistrodon halys</u>		
<b>Asia</b>			
Haffkine Biopharma- ceutical Corp., Ltd. Parel, Bombay India	<u>Bungarus caeruleus</u> <u>Naja naja</u> <u>Vipera russelli</u> <u>Echis carinatus</u>	Polyvalent	Digested with pepsin, concentrated and lyophilized.
Central Research Institute Kasauli, India	<u>Naja naja</u>	Anti-Naja	Enzyme-refined globulin in liquid and lyophilized forms.
	<u>Bungarus caeruleus</u>	Anti-Bungarus	
	<u>Vipera russelli</u>	Anti-Vipera	

SNAKE VENOM IMMUNOLOGY

57

producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<u>Asia</u>			
	<u>Echis carinatus</u>	Anti-Echis	
	<u>Naja naja</u>		
	<u>Bungarus caeruleus</u>		
	<u>Vipera russelli</u>	Polyvalent	
	<u>Echis carinatus</u>		
National Institute of Health Biological Products Div. Islamabad, Pakistan	<u>Vipera russelli</u>	Monovalent Vipera	
	<u>Echis carinatus</u>	Monovalent Echis	
	<u>Naja sp.</u>		
	<u>Bungarus sp.</u>		
	<u>Vipera russelli</u>	Polyvalent Anti-snake Serum	
	<u>Echis carinatus</u>		
Industrie and Pharma- ceutical Corporation Rangoon, Burma	<u>Naja n. kaouthia</u>	Mono-cobra	
	<u>Vipera russelli siamensis</u>	Mono-Vipera	
	<u>Naja n. kaouthia</u>		
	<u>Vipera russelli siamensis</u>	Biovalent	
Queen Saovabha Memorial Institute Rama 4 Road Bangkok, Thailand	<u>Bungarus fasciatus</u>	Bungarus	
	<u>Naja naja</u>	Cobra	
	<u>Ophiophagus hannah</u>	King Cobra	

(Continued)

Table 2 Continued.

Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<b>Asia</b>			
	<u>Vipera russelli</u>	Russell's Viper	
	<u>Agkistrodon*</u> <u>rhodostoma</u>	Malayan Pit Viper	
	<u>Trimeresurus albolabris</u>	Bivalent	
	<u>Trimeresurus erythrurus</u>		
	<u>*Calloselasma</u>		
Perusahaan Ibum Bio Farma (Pasteur Institute) Jl. Pasteur 20 P.O. Box 47 Bandung, Indonesia	Agkistrodon* rhodostoma <u>Bungarus fasciatus</u> <u>Naja spilatrix</u> <u>*Calloselasma</u>	Trivalent anti-venom serum	Purified serum supplied in liquid form.
Shanghai Vaccine and Serum Institute 1262 Yang An Road Shanghai, China	<u>Agkistrodon halys</u> <u>Agkistrodon acutus</u>	Manushi	precipitated with ammonium sulphate and lyophilized.
National Institute of Preventive Medicine 161 Kun-tang Street Nan-Kang, Taipei Taiwan	<u>Agkistrodon acutus</u> <u>Naja naja atra</u> <u>Bungarus multicinctus</u>	Agkistrodon Naja Bungarus	Immunized with formalin-toxoid venom. Ammonium sulphate precipitated, and supplied

RUSSELL

SNAKE VENOM IMMUNOLOGY

Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<b>Asia</b>			
	<u>Naja naja atria</u> <u>Bungarus multicinctus</u>	"Polyvalent neuro-toxic antivenins"	In liquid or lyophilized form.
	<u>Trimeresurus mucrosquamatus</u> <u>Trimeresurus gramineus</u>	"Polyvalent haemorrhagic antivenin"	
<hr/>			
The Chemo-Sero-Therapeutic Research Institute 668 Okubo Shimizu Kanamto 360, Japan	<u>Trimeresurus flavoviridis</u> <u>Akistrodon halys</u>	Habu Hamushi	Pepsin digestion, ammonium sulphate precipitation, and lyophilized.
<hr/>			
Takeda Chemical Industries, Ltd. Higashiku Osaka, Japan	<u>Akistrodon halys</u>	Hamushi	Pepsin digestion, ammonium sulphate precipitation, and lyophilized.
<hr/>			
Research Institute for Microbial Diseases Osaka University Kitaku Osaka, Japan	<u>Akistrodon halys</u>	Hamushi	Pepsin digestion, ammonium sulphate precipitation, and lyophilized.
<hr/>			
			(Continued)

Table 2 Continued.

Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<b>Asia</b>			
Kitasato Institute Minato-ku Tokyo, Japan	<u>Agiistrodon halys</u>	Mamushi	pepsin digestion, ammonium sulphate precipitation, and lyophilized.
Chiba Serum Institute 2-6-1 Konodai, Ichikawa Chiba, Japan	<u>Agiistrodon flavoviridis</u> (absorbed habu toxoid)	Habu	pepsin digestion, ammonium sulphate precipitation, and lyophilized.
Serum and Vaccine Laboratories Alabang Muntinlupa Rizal, Philippines	<u>Naja naja philippensis</u>	Cobra	Concentrated and purified.

SNAKE VENOM IMMUNOLOGY

61

Producer or Distributor	Venoms Used in Preparation	Trade or Common Name	Comments
<b>Australia</b>			
Commonwealth Serum Labs 45 Poplar Road Parkville, Victoria 3052 Australia	<u>Acanthophis antarcticus</u> <u>Notechis scutatus</u> <u>Enhydrina schistosa</u>	Death adder Tiger snake Sea snake	Prepared by pepsin digestion, and ammonium sulphate precipitation.
	<u>Oxyuranus scutellatus</u> <u>pseudonaja textilis</u>	Taipan Eastern brown snake	The products are dialyzed and ultra-filtered to a final concentration of 17% protein.
	<u>Pseudechis australis</u>	Brown snake or Mulga	
<b>Australia</b>			
	<u>Oxyuranus scutellatus</u> <u>Acanthophis antarcticus</u> <u>Notechis scutatus</u> <u>Pseudechis australis</u> <u>Pseudonaja textilis</u>	Polyvalent (Australia-New Guinea)	

should show efficacy for 10 or more years, but the legal complications attending their use beyond five years make it necessary to advise that the antivenin be discarded or used for laboratory research purposes. A listing of antivenin producers is shown in Table II.

Acknowledgements: The author wishes to express his appreciation for the advice and assistance of S. A. Minton, W. S. Jeter, N. B. Egen, F. J. McCarthy, N. C. Bucknall, M. R. Russell and C. Morrow. Part of this work was prepared while the author was the George C. Griffith Scholar of the American College of Physicians. Studies noted as unreported, 1984-1987, were supported by NS 17744 to the author and a grant from R. Sutro.

#### REFERENCES

1. Russell, F.E., Snake Venom Poisoning, Scholium International, Great Neck, New York, 1983.
2. Galen, in Opera omnia, edited by C.G. Kühn, C. Cnobloch, Lipsiae, 1821-33.
3. Apollodorus, Peri Therion, in Syrian Anatomy, Pathology and Therapeutics, or "The Books of Medicines", Oxford University Press, edited by E.A.W. Budge, London, 1913.
4. Nicander, Theriaca et Alexipharmacum, Aldum Marristium, Venetis, 1499.
5. Russell, F.E. and Scharffenberg, R.S., Bibliography of Snake Venoms and Venomous Snakes, Bibliographic Associates, Covina, California, 1964.
6. Paul of Aegina, The Seven Books of Paulus Aegineta, translated by F. Adams, Sydenham Society, London, 1844-47.
7. Reinach, T., Mithridates Eupator, Masson, Paris, 1890.
8. Russell, F.E., Confrontations in the Organization of Medicine during Tudor Times, unpublished data, 1987.

9. Lichtenhaeler, C., Thucydide a-t-il cru à la contagiosité de la "pente" d' Athènes? Gesnerus, 19:83, 1962.
10. Harvey, A.M., Snake venom and medical research - some contributions related to the Johns Hopkins University School of Medicine, Johns Hopkins med. J., 142:47, 1978.
11. Calmette, A., Les Venins, les Animaux Venimeux et la Séro-thérapie Antivenimeuse, Masson, Paris, 1907.
12. The Pharsalia of Lucan, translated by Edward Ridley, Longmanns, Green & Co., London, 1896.
13. Noguchi, H., Snake Venoms. An Investigation of Venomous Snakes with Special Reference to the Phenomena of their Venom, Carnegie Institute, Washington, DC, 1909.
14. Minton, S.A., Jr. and Minton, M.R., Venomous Reptiles, Scribners, New York, 1969.
15. Landois, L., Die Transfusion des Blutes, F.C.W. Vogel, Leipzig, 1875.
16. Libavius, A., Syntagma Areanorum et commentationum chymicorum, Frankfurt, 1613-15, 2 vols.
17. Giovanni Colle a Collibus, Methodus facile parandi jucunda, tuta et nova medicamenta, Venice, 1628.
18. Lowthrop, J., Anatomical, Medical and Chymical, and Philosophical and Miscellaneous Papers, in The Philosophical Transactions and Collections, vol. 3, Innys et al., London, 1668.
19. Folli, F., Stadera Medica, nella quale oltre, la medicina infusoria . . . del sanguis, Cecchi, Florence, 1680.
20. Lower, R. and King, E., An account of the experiments of transfusion, practiced upon a man in London, Phil. Trans., 2:557, 1667.
21. Denis, J.B., Lettre . . . touchant deux expériences de la transfusion faites sur des hommes, Cusson, Paris, 1667.
22. Kocher, P.H., John Hester, Paracelson (1576-93). John Quincy Adams Memorial Studies, Washington, 1948.
23. Ponfick, C., Experimentelle Beiträge zur Lehre von der Transfusion. Virchows Archiv., 62:273, 1875.

24. Jenner, E., An Inquiry Into the Causes and Effects of the Variolae Vaccinae, S. Law, London, 1798.
25. Rhazes, De variolis et morbillis commentarius, G. Bowyer, London, 1766.
26. Voltaire, F.M.A. de, The Complete Works of Voltaire, edited by T. Besterman, University of Toronto Press, Toronto, 1968.
27. Woodward, J., A State of Physick: and of Diseases . . . Particularly of the Small-pox, T. Horne, London, 1718.
28. Garrison, F.H., An Introduction to the History of Medicine, W.B. Saunders, Philadelphia, 1913.
29. Vollgnad, H., Globus vitulinus, Misc. Cumosa isive Ephem, nat. cur., 2:181, 1671.
30. Pyalarini, G., Nova et tuta variolas excitandi per transplantationem methodus; nuper inventa et in usum tracta, J.G. Hertz, Venetiis, 1715.
31. Jesty, B., "Dr. Jenner not the first English vaccinator," in Lancet, Nov. 27, 1869.
32. Thacher, T., A Brief Rule to Guide the Common-People of New-England How to Order Themselves and Theirs in the Small Pocks, or Measles, J. Foster, Boston, 1677.
33. Boylston, Z., An Historical Account of Small-pox Inoculated in New England, S. Chandler, London, 1726.
34. Mather, C., An Account of the Method and Success of Inoculating the Small Pox in Boston in New England, W. Owen, London, 1722.
35. Kirkpatrick, J., An Essay on Inoculation, Occasioned by the Small-Pox being brought into South Carolina in the Year 1738, J. Huggonson, London, 1743.
36. Mead, R., De variolis et morbillis liber, J. Brindley, Londini, 1747.
37. Franklin, B., Some Account of the Success of Inoculation for the Small-Pox in England and America, W. Strahan, London, 1759.
38. Dimsdale, T., The Present Method of Inoculating for the Small-pox, W. Owen, London, 1767.

39. Waterhouse, B., A Prospect of Exterminating the Small-pox, W. Hilliard, Boston, 1800-02.
40. Pasteur, L., Sur les maladies virulentes, et en particulier sur la maladie appelée vulgairement choléra de poules, C.R. Acad. Sci. (Paris), 90:239, 1880.
41. Pasteur, L. and Chamberland, C., Sur l'etiology du charbon, C.R. Acad. Sci. (Paris), 92:1378, 1881.
42. Roux, P.P.E. and Yerson, A.E.J., Contribution à l'étude de la diphthérie, Ann. Inst. Pasteur, 2:629, 1888.
43. Von Behring, E.A. and Kitasato, S., Ueber das Zustandekommen der Diphtherie-immunität un der Tetanus-immunität bei Thieren, Deutsch. med. Wochenschr., 16:1113, 1890.
44. Ehrlich, P., Gesammelte Arbeiten ueber Immunitätsforschung, A. Hirschwald, Berlin, 1904.
45. Metchnikoff, E., Ueber eine Sprosspelzkrankheit der Daphnien, Virchows Arch. Path. Anat., 96:177, 1884.
46. Sewall, H., Experiments on the preventive inoculation of snake venom, J. Physiol., 8:203, 1887.
47. Calmette, J., Les Venins, Lex Animaux Venimeux et La Sérothérapie Antivenimeuse, Masson, Paris, 1907.
48. Krehl, L., Lehrbuch der inneren medizin, G. Fisher, Jena, 1908.
49. Mitchell, S.W. and Reichert, E.T., Preliminary report on the venoms of serpents, Med. News, 42:3, 1883.
50. Mitchell, S.W. and Reichert, E.T., Researches Upon the Venoms of Poisonous Serpents, Smithsonian Contribution to Knowledge, Washington, 26:647, 1886.
51. Wolfenden, R.N., On the nature and action of the venoms of poisonous snakes, J. Physiol., 7:327, 1886.
52. Kaufmann, M., Du Venin de la Vipère, Masson, Paris, 1889.
53. Calmette, A., Étude expérimentale du venin de Naja tripudians, Ann. Institut Pasteur, 6:160, 1892.
54. Kanthack, A.A., Report on snake venom in its prophylactic relation with poisons of the same and other sorts, Rep. Med. Off. Local Govt. Bd., 1895-6, London, 1897.

55. Phisalix, M.M.C. and Bertrand, G., Sur la propriété anti-toxique du sang des animaux vaccinés contre le venin de vipére, C.R. Acad. Sci., 68:356, 1894.
56. Phisalix, M.M.C. and Bertrand, G., Recherches sur l'immunité du hérisson contre le venin de vipére, Comp. Rendus Soc. Biol., 2:639, 1895.
57. Calmette, A., Propriétés du sérum des animaux immunisés contre le venin des serpents, et thérapeutique de l'envenimation, C.R. Acad. Sci., 68:720, 1894.
58. Fraser, T.R., The treatment of snake poisoning with anti-venene derived from animals protected against serpent's venom, Brit. med. J., II:416, 1895.
59. Fraser, T.R., [Professor Fraser shows a rabbit immunized against cobra poison.], Trans. Med. Chir. Soc. Edinburgh, 14:212, 1895.
60. Stephens, T., On the haemolytic action of snake toxins and toxic sera, J. Path. Bact., 6:273, 1900; see also J. Path. Bact., 5:279, 1898.
61. Meyers, A.B., On the interaction of toxin and antitoxin; illustrated by the reaction between cobralysin and its antitoxin, J. med. Res., 6:363, 1904.
62. McFarland, J., Some studies of venoms and antivenes, Proc. Path. Soc. Phila., 1900; Proc. Soc. Amer. Bact., 1900; Proc. Am. med. Assoc., 1901; J.A.M.A., 1901; see Phila. med. J., 9:329, 1902.
63. Tidswell, F., Researches on Australian Venoms, Gullick, Sydney, 1906.
64. Flexner, S. and Noguchi, H., The constitution of snake venom and snake sera, U. Penn. med. Bull., 15:345, 1902.
65. Flexner, S. and Noguchi, H., Snake venom in relation to haemolysis, bacteriolysis, and toxicity, J. exp. Med., 6:277, 1903.
66. Flexner, S. and Noguchi, H., Upon the production and properties of anticrotalus venin, J. med. Res., 11:363, 1904.
67. Lamb, G., Specificity of antivenomous sera, Sci. Mem. Off. Med. Sanit. Dept. Govt. India, 5:1, 1903; 10:1, 1904.

68. Lamb, G., The specificity of antivenomous sera with special reference to a serum prepared with the venom of Daboia russelli, Sci. Mem. Off. Med. Sanit. Dept. Govt. India, 16:1, 1905.
69. Brazil, V., Contribution à l'étude d'origine ophidienne, A. Maloine, Paris, 1905.
70. Ishizaka, T., Studien ueber das Habuschlängengift, Zeit. exp. path. Therap., 4:88, 1907.
71. Kitashima, T., On "Habu" venom and its serum therapy, Philippine J. Sci., 8., Med. Sci., 3:151, 1908.
72. Phisalix, M., Les Animaux Venimeux et les Venins, Masson, Paris, 1922.
73. Pavlovsky, E.N., Gifftiere und Ihre Giftigkeit, G. Fischer, Jena, 1927.
74. Boquet, P., Venins de Serpents, Institut Pasteur, Paris, 1963.
75. Boquet, P., Izard, Y., Jouannet, M. and Meaume, J., Studies on some antigenic proteins and polypeptides from Naja nigricollis venom, in Animal Toxins, edited by F.E. Russell and P.R. Saunders, Pergamon Press, Oxford, 1967.
76. Boquet, P., Observations on anti-venom immunity, in Toxins of Animal and Plant Origin, edited by A. de Vries and E. Kochva, vol. 3, p. 823, Gordon and Breach, New York, 1973.
77. Boquet, P., Dumarey, C. and Joseph, D., The problem of the antigenicity of some short toxins of Elapidae and Hydrophiidae venoms, in Toxins - Animal, Plant and Microbial, edited by P. Rosenberg, p. 71, Pergamon Press, Oxford, 1978.
78. Boquet, P., History of snake venom research, in Snake Venoms, edited by C.-Y. Lee, p. 3, Springer-Verlag, Berlin, 1979.
79. Minton, S.A., An immunological investigation of rattlesnake venoms by the agar diffusion method, Am. J. Trop. Med. Hyg., 6:1097, 1957.
80. Minton, S.A., Observations of toxicity and antigenic makeup of venoms from juvenile snakes, in Animal Toxins, edited by F.E. Russell and P.R. Saunders, p. 211, Pergamon Press, Oxford, 1967.

81. Minton, S.A., Paraspecific protection by elapid and sea snake antivenins, Toxicon, 5:47, 1967.
82. Minton, S.A., Common Antigens in snake venoms, in Snake Venoms, edited by C.-Y. Lee, p. 847, Springer-Verlag, Berlin, 1979.
83. Minton, S.A., Weinstein, S.A. and Wilde, C.E., An enzyme-linked immunoassay for detection of North American pit viper venoms, J. Tox. Clin. Tox., 22:303, 1984.
84. Grohmann, W., Ueber die Einwirkung des zellenfreien Blutplasma auf einige pflanzliche Microorganismen (schimmel-, spross-, pathogene and nichtpathogene Spaltpilze), C. Mattiesen, Dorpat, 1884.
85. Buchner, H., Ueber die bakterientötende Wirkung des zellenfreien Blutserums, Zentralbl. Bakteriol., 5:817, 1889.
86. Bordet, J., Les Leucocytes et les propriétés actives du sérum chez les vaccinés, Ann. Inst. Pasteur, Paris, 9:462, 1895.
87. Ehrlich, P. and Morgenroth, J., Zur Theorie der Lysin-Wirkung, Berl. klin. Wschr., 36:6, 1899.
88. Bordet, J. and Gengou, O., Sur l'existence de substances sensibilisatrices dans la plupart des sérums antimicrobiens, Ann. Inst. Pasteur Paris, 15:289, 1901.
89. Ferrata, A., Die Unwirksamkeit der komplexen Hämolsine in salzfreien Lösungen und ihre Ursache, Berl. klin. Wschr., 44:366, 1907.
90. Brand, E., Ueber das Verhalten der Komplemente bei der Dialyse, Berl. klin. Wschr., 44:1075, 1907.
91. Gordon, J., Whitehead, H.R. and Wormall A., The action of ammonia on complement. The fourth component. Biochem. J. 20:1028, 1926.
92. Fontana, F., Richerche fisiche sopra il veleno della vipera, Giusti, Lucca, 1767.
93. Ewing, C.B., The action of rattlesnake venom upon the bacterialcidal power of the blood serum, Lancet, 1:1236, 1894.
94. Stephens, T.W.W. and Myers, W., Test-tube reactions between cobra poison and its antitoxin, Br. med. J., 1:620, 1898; see also J. Path. Bact., 5:279, 1898.

95. Kyes, P., Ueber die Wirkungsweise des Cobragiftes, Berl. klin. Work., 39:886, 1902.
96. Kyes, P. and Sachs, H., Zur Kenntnis der Cobragiftaktivierenden Substanzen, Berl. klin. Wochenschr., 40:21, 1903.
97. Noc, F., Sur quelques propriétés physiologiques des différents venins de serpents, Ann. Inst. Pasteur, 18:307, 1904.
98. Von Dungern and Coca, A.F., Ueber Hämolyse durch Schlangengift, Biochem., 2(12):407, 1908.
99. Morgenroth, J. and Kaya, R., Über eine komplementzerstörende Wirkung des Kobragiftes, Biochem., 2(8):378, 1908.
100. Sachs, H. and Amorokow, L., Über die Wirkung des Cobragiftes auf die Komplemente, II. Mitteilung, 2, Immun.-Forsch., 11:710, 1911.
101. Ritz, H., Über die Wirkung des Cobragiftes auf die Komplemente. III. Mitteilung Zugleich ein Beitrag zur Kenntnis der hämolytischen Komplemente, 2, Immun.-Forsch., 13:62, 1912.
102. Coca, A.F., A study of the anticomplementary action of yeast, of certain bacteria and of cobravenuom, 2, Immun.-Forsch., 31:604, 1904.
103. Pillemer, L., Blum, L., Lepow, I.H., et al., The properdin system and immunity I. Demonstration and isolation of a new serum propeptin, properdin, and its role in immune phenomena, Science, 120:279, 1954.
104. Vogt, W. and Schmidt, G., Abtrennung des anaphylatoxinbildenden Prinzips aus Cobragift von anderen Giftkomponenten, Experientia (Basel), 20:207, 1964.
105. Alper, C.A., Colten, H.R., Gear, et al., Homozygous human C3 deficiency. The role of C3 in antibody production. C1s-induced vasopermeability, and cobra venom-induced passive hemolysis, J. clin. Invest., 57:222, 1976.
106. Alper, C.A. and Balavitch, D., Cobra venom factor: evidence for its being altered cobra C3 (the third component of complement), Science, 191:1275, 1976.
107. Alper, C.A., Colten, H.R., Gear, J.S.S., et al., Homozygous human C3 deficiency. The role of C3 in antibody production, C1s-induced vasopermeability and cobra venom-induced passive hemolysis, J. clin. Invest., 57:222, 1976.

108. Alper, C.A., Snakes and the complement system, in Snake Venoms, edited by C.-Y. Lee, Chapt. 22, Springer-Verlag, Berlin, 1977.
109. Lamb, G., On the precipitin of cobra venom, Lancet, II:431, 1902.
110. Muelling, R.J., Samson, R.F. and Bevan, T., The precipitin test elucidating the cause of death, Am. J. Clin. Path., 28:489, 1957.
111. Russell, F.E., Gel diffusion study on human sera following rattlesnake venom poisoning, Toxicon, 4:147, 1967.
112. Trethewie, E.R. and Rawlinson, P.A., Immunological diagnosis of type of snake in snakebite, Med. J. Australia, 2:111, 1967.
113. Boche, R.D. and Russell, F.E., Passive hemagglutination studies with snake venom and antivenin, Toxicon, 6:125, 1968.
114. Russell, F.E., Experiences with passive hemagglutination testing in snake venom poisoning, Grand Rounds Bulletin, Los Angeles Country/University of Southern California Medical Center, 37:2, 1978; see also reference 1.
115. Theakston, R.D.G., The application of immunoassay techniques including enzyme-linked immunoassay (ELISA) to snake venom research, Toxicon, 21:341, 1983.
116. Trethewie, E.R., Detection of snake venom in tissues, Clin. Tox., 3:445, 1970.
117. Knight, B., Barclay, A. and Mann, R., Suicide by injection of snake venom, Forensic Sci., 10:141, 1977.
118. Yadlowski, J.M., Tu, A.T., Garriott, J.C. and Norton, L.E., Suicide by snake venom injection, J. Forensic Sci., 25:760, 1980.
119. Russell, F.E., Snake venom poisoning, in Cyclopedia of Medicine, Surgery and the Specialties, edited by G.M. Piersol, Vol. 2, p. 197, F.A. Davis, Philadelphia, 1962.
120. Tiru-Chelvam, R., Demonstration of sites of snake-venom localisation by immunofluorescence techniques, J. Path., 107:303, 1972.

121. Greenwood, B.M., Warrell, D.A., Davidson, N.M., Ormerod, L.D. and Reid, H.A. Immunodiagnosis of snakebite, Br. med. J., 4:743, 1974.
122. Coulter, A.R., Sutherland, S.K. and Broad, A.J., Assay of snake venoms in tissue fluids, J. Immunol. Methods, 4:297, 1974.
123. Sutherland, S., Coulter, A.R., Broad, A.J., Hilton, J.M.N. and Lane, L.H.D., Human snake bite victims: the successful detection of circulatory snake venom by radioimmunoassay, Med. J. Australia, 1:27, 1975.
124. Coulter, A.R., Cox, J.C., Sutherland, S.K. and Waddell, C.J., A new solid-phase sandwich radioimmunoassay and its application to the detection of snake venom, J. Immunol. Methods, 23:241, 1978.
125. Coulter, A.R., Cox, J.C., Sutherland, S.K. and Waddell, C.J., [Experiences with 70 cases of snakebite, using the RIA.] Noted in reference 124.
126. Nakane, P.K. and Pierce, G.B., Jr., Enzyme-labeled antibodies; preparation and application for the localization of antigen, J. Histochem. Cytochem., 14:929, 1966.
127. Massayeff, R. and Maiolini, R., A sandwich method of enzyme immunoassay. Application to rat and human alpha fetoprotein, J. Immunol. Methods, 8:223, 1975.
128. Theakston, R.D.G., Lloyd-James, M.J. and Reid, H.A., Micro-ELISA for detecting and assaying snake venom and venom-antibody, Lancet, II:639, 1977.
129. Pugh, R.N.H. and Theakston, R.D.G., Incidence and mortality of snake bite in Savanna Nigeria, Lancet, Nov. 29, p. 1181, 1980.
130. Coulter, A.R., Harris, R.D. and Sutherland, S.K., Enzyme immunoassay for the rapid clinical identification of snake venom, Med. J. Australia, 1:433, 1980.
131. Theakston, R.D.G., Lloyd-James, J.M. and Reid, H.A., Micro-ELISA for detecting and assaying snake venom and venom-antibody, Lancet, II:639, 1977.
132. Pearn, J., Morrison, J., Charles, N. and Muir, V., First-aid for snake-bite: efficacy of a constrictive bandage with limb immobilization in the management of human envenomation, Med. J. Australia, 2:293, 1981.

133. Gopalakrishnakone, P., Hawgood, B.J. and Theakston, R.D.G., Specificity of antibodies to the reconstructed crototoxin complex, from the venom of South American rattlesnake (*Crotalus durissus terrificus*) using enzyme-linked immunosorbent assay (ELISA) and double immunodiffusion, Toxicon, 19:131, 1981.
134. Tzeny, M.C. and Shiek, W.R., Enzyme immunoassay of cobrotoxin and antcobrotoxin antibodies, J. Clin. Biochem. Soc. 10:53, 1981.
135. Lwin, K.O. and Myint, A.A., The use of enzyme-linked immunosorbent assay (ELISA) in detection of Russell's viper venom in body fluid, Snake, 14:77, 1982.
136. Chandler, H.M. and Hurrell, G.R., A new enzyme immunoassay system suitable for field use and its application in a snake venom detection kit, Clin. Acta, 121:225, 1982.
137. Minton, S.A., Weinstein, S.A. and Wilde, C.E., An enzyme-linked immunoassay for detection of North American pit viper venoms, J. Toxicol. Clin. Toxicol., 22:303, 1984.
138. Banner, W., Russell, F., Barton, B. and Schwager, E., Fatal rattlesnake bite in a child, Vet. Hum. Toxicol., 26(5):400, 1984.
139. Hitt, J.M., Determination of the efficacy of the immunosorbent assay (ELISA) in characterizing *Crotalus* snake venom at the species level. Thesis, University of Arizona, Tucson, 1986.
140. Russell, F.E., Sullivan, J.B. and Egen, N.B., et al., Preparation of a new antivenin by affinity chromatography, Am. J. Trop. Med. Hyg., 34:141, 1985.
141. Gringrich, W.C. and Hohenadel, J.C., Standardization of polyvalent antivenin, in Venoms, edited by E.E. Buckley and N. Porges, p. 381, AAAS, Washington, 1956.
142. Hitt, J.M. and Russell, F.E., Study of crotalid venoms at the subspecies level using the ELISA, unpublished data, 1986.
143. Minton, S.A., Present tests for detection of snake venoms: clinical applications, represented at UA/EM-IRIEM Research Symposium, Clearwater, Florida, February, 1987.
144. Hunter, A., On the precipitins of snake antivenoms and snake antisera, J. Physiol., 33:239, 1905.

145. Githens, T.S. and Buty, L.W., Venoms of North American snakes and their relationships, J. Immunol., 16:71, 1929.
146. Githens, T.S. and Wolff, N.O.C., The polyvalency of crotalidae antivenins, J. Immunol., 37:33, 1939.
147. Picado, C., Venom of Costa Rican arboreal vipers, Bull. Antivenin Inst. Amer., 4:1, 1930.
148. Akatsuka, K., Immunological studies of snake venoms, Jap. J. exp. Med., 14:147, 1936.
149. Kellaway, C.H., The specificity of active immunity against snake venoms, J. Path. Bact., 33:157, 1930.
150. Taylor, J. and Mallick, S.M.K., Observations on the neutralization of the haemorrhagin of certain viper venoms by antivenene, Indian J. med. Res., 23:127, 1935.
151. Ahu Ja, M.L., Specificity of antivenomous sera with special reference to sera prepared with venoms of Indian and South African snakes, Indian J. med. Res., 22:479, 1935.
152. Grasset, E. and Schaafsma, A.W., Antigenic characteristics of boomslang (Dispholidus typus) venom and preparations of a specific antivenene by means of formalized venom, S. Afr. med. J., 14:484, 1940.
153. Russell, F.E. and Egen, N.B., unpublished data, 1985.
154. Russell, F.E., Timmerman, W.F. and Meadows, P.E., Clinical use of antivenin prepared from goat serum, Toxicon, 8:63, 1970.
155. Russell, F.E., Pharmacology of venoms, in Natural Toxins, edited by D. Eaker and T. Wadstrom, Pergamon Press, Oxford, 1980.
156. Criley, B.R., Development of multivalent antivenin for the family Crotalidae, in Venoms, edited by E.E. Buckley and N. Porges, p. 373, A.A.A.S., Washington, 1956.
157. Christensen, P.A., South African Snake Venoms and Antivenoms, South African Institute Medical Research, Johannesburg, 1955.
158. W.H.O. Coordinated meeting on Venoms and Antivenoms, WHO/BS/80-1292/BLG/VEN/80.1 Rev. 1, 1980.

## APPENDIX: GLOSSARY OF TERMS

ACQUIRED IMMUNITY: Immunologic resistance developed after birth as a result of previous exposure. Sometimes referred to as "specific active immunity".

ACTIVE IMMUNIZATION: Induction of a state of immunity, usually to a specific antigen, produced by the individual's or animal's own immune system.

ADJUVANT: A substance that can increase the specific production of an antibody to an antigen by increasing its size or length of survival in the circulation.

AFFINITY: The intrinsic binding power of an antibody-combining site with an antigenic substrate binding site.

AGGLUTINATION: Antigen-antibody reaction in vitro in which contact results in aggregates or clumps.

AGGLUTININ: A multivalent molecule that causes agglutination by direct interaction with its corresponding antigen. IgM is a particularly potent agglutinin.

ALLELLE: An inherited variant of a gene.

ALLERGEN: A substance capable of inducing an allergic reaction.

ALLERGIC: A state of altered reactivity, generally denoting hypersensitivity.

ALLERGY: An immune reaction resulting in a reaction to some tissues or cells, usually through a hypersensitivity reaction.

ALLOGENIC: Having a different genetic constitution, usually used to describe intraspecies antigenic differences (xenogeneic).

**ALLOSTERIC TRANSFORMATION:** The binding of C1 to the antigen-antibody complex, resulting in a shape change that exposes a new site (allosteric site) by which it can react with another complement protein (C4).

**ALLOTYPE:** A genetic marker at an individual locus, usually inherited as alternatives.

**ANAPHYLAXIS:** A state of severe hypersensitivity to a foreign substance caused by the release of vasoactive amines, and triggered by the interaction of cell-bound antibody with the antigen.

**ANAPHYLATOXINS:** Substances that degranulate mast cells on being released during an anaphylactic reaction. Histamine and serotonin are major anaphylotoxins.

**ANERGY:** Absence of immunological reactivity.

**ANTIBODY:** A molecule produced in response to exposure to an antigen and which has the property of combining specifically with that antigen at its antigen-combining site.

**ANTIGEN:** A substance of relatively high molecular weight that is capable of mitigating the production of an antibody specific to itself.

**ANTIVENIN (ANTIVENENE, ANAVENIN, ANTIVENIMEUX, ANTIVENINIUM, ANTIVENOM):** An antitoxin prepared by immunizing animals against a specific venom or venoms, processing the sera, and preparing it for use in humans or other animals. Antivenin is preferred to the other terms on the basis of historical precedent and the implication that it identifies a specific technique, that is, the immunization of animals. The term antivenom is frequently employed to denote any substance that has an action against a

venom, such as tannic acid, extracto de guaco, KM<sub>n</sub>O<sub>4</sub>, strychnine, musk, or any other substance. Antivenin also enjoys a far more world-wide usage than the other words. For these reasons anti-venin seems a more appropriate and less confusing term.

**ANTIVENIN INDEX:** A listing of the antivenins available in zoos and universities throughout the United States for the treatment of native and exotic snakes.

**ATTENUATED:** To be rendered less virulent.

**AUTOANTIBODY:** An antibody directed against self antigens (autoantigens).

**AVIDITY:** The combining power of an antibody with its antigen; related to the affinity and the valencies of the antibody and its antigen.

**BLOCKING ANTIBODY:** An "incomplete" antibody capable of coating the red cell determinant to render it partially or completely blocked and inagglutinable by antibodies of the same specificity.

**CAPPING:** The process of redistribution of cell-surface determinants to one small part of the cell surface.

**CARRIER:** An immunogenic molecule to which a hapten is coupled in such a way as to induce an immunological response.

**CLONE:** A family of cells or organisms of identical genetical constituents derived asexually from a single cell by repeated division.

**COBRA VENOM FACTOR (CVF):** A C3b analogue isolated from cobra venom. It has the property of activating the 'alternative pathway' of complement activating and destroying C3-C9.

COLD AGGLUTININ: An agglutinin whose optimum temperature of reactivity is in the cold, whose potency decreases with increases in temperature, and whose reaction at 37°C is usually negative.

COMPLEMENT: A complex group of 11 distinct glycoproteins found in the blood serum and other body fluids that react with one another sequentially in a cascading reaction to form potent biological effects, including immune adherence, phagocytosis and cell lysis. Complement factors are designated by the letter C: C<sub>1</sub>, C<sub>2</sub>, etc. C<sub>1</sub> is composed of three subunits: C<sub>1q</sub>, C<sub>1r</sub>, and C<sub>1s</sub>. Activation of the complement system occurs with IgM or IgG. Chemically, these proteins are fairly large molecules, 75,000 - 240,000 daltons.

COMPOUND ANTIGEN: A combination of more than one antigen against which a single antibody appears to be directed.

CYCLIC AMP: An intracellular mediator having a particularly important effect on the activity of microtubules and other contractile elements of a cell.

CYTOPHILIC: Having an affinity for cells. Usually applied to antibodies which bind to macrophages.

DOUBLE DIFFUSION: Immunochemical analysis of antigenic relationships, pioneered by Ouchterlony.

EFFECTOR CELL: A cell actually carrying out a specific function, such as cell-mediated cytotoxicity.

ELISA: An acronym for enzyme-linked immunosorbent assay. This assay utilizes the principle of a solid phase (e.g., beads or microtiter plate wells) coated with antigen or antibody and an indicator reagent, antibody or antigen, respectively, to which an enzyme has been conjugated or "linked".

ENDOTOXIN: Lipopolysaccharides localized in cell walls.

EXOTIC SNAKES: Foreign, or those non-native to the United States.

Fab FRAGMENT: The fragment of the antibody molecule capable of antigen binding.

FREUND'S ADJUVANT: A water-oil emulsion of antigen-killed M. tuberculosis, usually in the oily phase (complete Freund's adjuvant). Incomplete Freund's adjuvant contains no organisms in the oil phase.

HAPten: A small molecule which will combine with antibody but which is not capable of evoking an antibody response in itself.

HEMAGGLUTININ: A molecule capable of agglutinating red blood cells.

HETEROLOGOUS: Usually used to denote inter-species antigenic differences.

IDIOTYPE: An antigenic marker for the antibody combining site. The antigen is found in the region of the antibody secreted by a single clone of lymphoid cells. Antibodies of different specificities have different idiotypes.

IgG: The predominant immunoglobulin class present in human serum.

IMMUNE ADHERENCE: A "glue-like" phenomenon occurring when a particular antigen, its homologous antibody, and complement unite.

IMMUNITY: Resistance to extraneous, foreign matter as determined by the immune system.

IMMUNOCOAGULININS: Antibodies (often autoantibodies) formed to complement components or their breakdown products, often autoantibodies.

IMMUNOFLUORESCENCE: The method involving the use of fluorochrome-labelled antibody to cellular determinants.

IMMUNOGENIC: Producing immunity. Autogenic.

IMMUNOGENICITY: The ability of an antigen to stimulate antibody production.

IMMUNOGLOBULIN: An antibody containing globulins, including those proteins without apparent antibody activity.

IMMUNOLOGIC ENHANCEMENT: The prolongation of the survival of an allograft from the action of a humoral antibody as against donor-histocompatible antigens that are lacking in the host.

INCOMPLETE ANTIBODY: An antibody that sensitizes red cells suspended in saline but fails to agglutinate them.

INHIBITION: The blocking of the normal reaction between an antigen and its corresponding antibody.

ISOANTIBODY: An antibody that reacts with an antigen present in another member of the same species but not in the animal itself.

ISOANTIGEN: An antigen that elicits antibody formation in another member of same species not genetically identical.

MAJOR CROSMATCH: A compatibility test used to detect the presence of antibody in the recipient's serum: donor's red cells versus recipient's serum.

MINOR CROSMATCH: A compatibility test used to detect the presence of antibody in the donor's serum: donor's serum versus recipient's red cells.

MONOCLONAL: Derived from a single-cell clone, usually immunoglobulin, to denote unusual homogeneity.

MONOVALENT: A single antigen or antibody. In general, monovalent antivenins are prepared with the venom of a single species of snake, although the antivenin may mitigate the effects of antigens of several or more snakes of the same or closely related genera.

NATURALLY OCCURRING ANTIBODIES: Antibodies that occur without an apparent stimulus. Also known as non-red-cell-immune antibodies or innate antibodies.

PANAGGLUTINATION: The reaction of red cells, irrespective of blood group, with all human sera.

PASSIVE ANTIBODY: An antibody which, when injected into an individual, provides temporary immunity.

PHAGOCYTOSIS: Ingestion of a solid or semisolid material into a cell by closing off an invagination of the protoplasm. The process requires the activity of contractile elements of the cells and aerobic respiration. The contents of the phagosome are usually digested by the discharge of cathepsins and other enzymes into the phagosome.

PLASMA CELLS: A terminally differentiated antibody-forming cell with a short half-life.

POISONOUS ANIMAL: Those creatures whose tissues, either in part or in their entirety, are toxic. Poisoning by these animals usually takes place through ingestion of their flesh. Sometimes called cryptotoxic animals.

POLYAGGLUTINATION: The agglutination of red cells by most human sera, irrespective of blood group.

POLYVALENT: Referring to several or many antigens or antibodies, often of different species, genera or even families.

PRECIPITATION: The reaction of soluble antigens with antibody, resulting in arcs or flocculation of the complexes in a gel medium.

PRECIPITIN: An antibody that reacts with its corresponding antigen to form a precipitate.

PRIMARY RESPONSE: The initial response to a foreign antigen.

PSEUDOAGGLUTINATION: The clumping of cells caused by agents other than antibodies.

PYROGENS: Thermostable, filter-passing substances that may cause febrile reactions when injected into a recipient. Probably of bacterial origin.

REAGENT RED CELLS: Red cells used in the laboratory for testing purposes.

RIA: A variety of immunological methods in which a radioactive isotope is used to detect antigens or antibodies.

SALINE ANTIBODY: An antibody that reacts with saline-suspended red cells.

SENSITIZATION: Stimulation by an antigen that renders a person liable to form antibodies.

SPECIES-SPECIFIC: Antigens or antibodies restricted to a particular species.

SPECIFICITY: The affinity between an antigen and its corresponding antibody.

SUBGROUPS: With respect to antigens or antibodies, subdivisions; often weakened forms.

SYNERGISM: The cooperative action between venom components.

TOLERANCE: A state of specific immunological unresponsiveness induced by exposure to antigen.

TOXIN: A substance derived from the tissues of a plant, animal, or microorganism which has a deleterious effect on another plant or animal. The word is usually used to denote a venom or poison fraction, although it is sometimes used to indicate the whole venom.

TOXOID: Toxins that have been modified to minimize their deleterious effects, while still retaining their immunogenic and antigenic properties.

VACCINATION: The inoculation or ingestion of organisms or antigens to produce immunity to those organisms or antigens in the recipient.

VENOMOUS ANIMAL: An animal having a venom gland or highly specialized group of secretory cells, a venom duct (although this is not a consistent finding), and a structure for delivering the venom, such as a sting, tooth or fang.

WARM ANTIBODY: An antibody that reacts optimally at 37°C.